REMARKS

The specification has been amended to correct inadvertent errors. No new matter has been added. Claim 4 was amended to correct a typographical error. This amendment was not necessitated by compliance with the statutory requirements for a patent and the scope of this claim has not been narrowed by the amendment thereto. New claims 12-15 were added. Support for these claims may be found at least in the originally filed claims, at page 14, lines 17-27 and at page 15, lines 1-20. No new matter was added. Claims 1-15 now are pending in the application.

Claims 1-11 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Jacobs et al., U.S. Patent No. 5,707,829, in view of Ducheyne et al., U.S. Patent No. 5,236,458. Applicants respectfully traverse this rejection.

Independent claim 1 is directed to a composition comprising particles of bioactive glass with a particle size less than about 20 μm in diameter and a suitable carrier for oral, intramuscular, intraperitoneal or intravenous administration. Independent claim 11 is directed to a composition comprising particles of a material with a particle size less than about 20 μm which biodegrades, produces elevated serum concentrations of calcium and phosphorous ions, does not cause elevated plasma TNF-α concentrations, and does cause elevated plasma IL-6 concentrations, in combination with a suitable carrier for oral, intramuscular, intraperitoneal or intravenous administration.

Method claim 8 is directed to a method for systemically minimizing the production of TNF-α caused by an inflammatory response in a patient comprising orally or intravenously administering an effective TNF-α lowering amount of bioactive glass particles with a size less than about 20 μm to the patient. Claim 10 is directed to a method for systemically increasing IL-6 levels in a patient, comprising administering to the patient an effective, IL-6 increasing amount of bioactive glass

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particles with a size less than about 20 μm.

Applicants have discovered that the compositions and methods of the invention can suppress plasma concentrations of tissue necrosis factor-alpha (TNF-α) while increasing plasma concentrations of interleukin-6 (IL-6).

Jacobs describes DNA sequences and secreted proteins encoded by the DNA sequences. A protein as detailed in Jacobs may be used to suppress chronic or acute inflammation such as that resulting from over production of cytokines such as TNF or IL-1. *Column 10, lines 51-57.* The proteins described may be used in pharmaceutical compositions which may also contain cytokines, lymphokines, or other hematopoietic factors such as M-CSF, GM-CSF, TNF, IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, IL-13, IL-14, IL-15, IFN, TNF0, TNF1, TNF2, G-CSF, Meg-CSF, thrombopoietin, stem cell factor, and erythropoietin. *Column 16, lines 36-42.* The protein of the Jacobs patent may be used with other therapeutically useful agents for compositions of the present invention which are useful for bone, cartilage, tendon or ligament regeneration. For such purposes, the composition preferably would include a matrix capable of delivering the protein-containing compositions to the site of bone and/or cartilage damage, providing a structure for the developing bone and cartilage. *Column 19, lines 16-37.* Such matrices may be chemically defined calcium sulfate, tricalciumphosphate, hydroxyapatite, polylactic acid, polyglycolic acid and polyanhydrides. Others may be sintered hydroxyapatite, bioglass, aluminates or other ceramics. *Column 19, lines 41-51.*

Jacobs describes a particular protein which may be used with other therapeutic agents. Jacobs does not describe a composition comprising bioactive glass with a particle size less than about 20 μm in diameter and a suitable carrier. Rather, Jacobs describes a matrix which delivers protein-containing compositions. The matrix is merely a delivery device and may be a variety of materials. Further, Jacobs does not describe minimizing the production of TNF-α by administering

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bioactive glass of a certain particle size. Jacobs additionally does not describe a method for systemically increasing IL-6 levels by the methods claimed. As pointed out in the Office Action, it is the protein of the Jacobs invention which suppresses chronic or acute inflammation, not the matrix or a material as presently claimed.

The Ducheyne patent describes bioactive material for a prosthesis or composite implants. The addition of the Ducheyne patent to the Jacobs patent does not remedy the deficiencies of the Jacobs patent. Neither cited patent provides information that would have led one of skill in the art to the compositions and methods claimed using bioactive glass. Ducheyne does not disclose bioactive glass for minimizing the production of TNF-α or increasing IL-6 levels. Jacobs discloses a protein which may suppress chronic or acute inflammation, but does not describe the use of bioactive glass therefore. Moreover, neither patent describes bioactive glass of a certain particle size and a carrier. Since the cited art would not have made the claimed invention obvious, Applicants respectfully request that this rejection be withdrawn.

Applicants note that the Information Disclosure Statement filed January 19, 2001, has not been acknowledged by providing Applicants with an initialed copy of the PTO-1449. Applicants respectfully request that an Examiner initialed copy of this form be returned to the undersigned.

Applicants believe they have responded to all matters raised in the above referenced Office Action and that the application is now in condition for allowance. If the Examiner has any questions concerning this Application or this Reply and Amendment, the Examiner is invited to contact the undersigned.

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Respectfully submitted,

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